Coronary artery stenting

David R Ramsdale

Coronary artery stenting minimizes the occurrence of abrupt closure and late restenosis after angioplasty. The range of stents now available allows interventional cardiologists to perform more complex angioplasties at lower risk. In the near future, biologically inert, biodegradable stents coated with antiproliferative and antithrombotic agents may become available.

Percutaneous transluminal coronary angioplasty (PTCA) has two limitations — abrupt vessel closure (2–5%) during or shortly after the procedure and restenosis as a result of fibrointimal hyperplasia (25–35%) occurring within the first 6 months of follow-up. Intracoronary artery stenting has been shown to reduce the frequency of both these complications and is now used in 60–95% of PTCA procedures.

HISTORY

Jacques Puel is credited with the first human coronary artery stent implantation in 1986 (Puel et al, 1987). In 1987, Ulrich Sigwart reported the use of the Medivent (self-expanding Wallstent) stent in a series of 19 patients to treat acute closure after PTCA and to prevent restenosis (Sigwart et al, 1987). The results in reestablishing coronary artery flow after abrupt closure were impressive and interventionists enthusiastically sought to use them for this 'bail-out' indication rather than opt for emergency coronary artery bypass surgery.

However, acute stent thrombosis leading to acute myocardial infarction and death was reported in a significant proportion of cases causing serious concern (Serruys et al, 1991). To solve this problem, aggressive anticoagulant therapy with aspirin, dipyridamole, or intravenous heparin, dextran and oral anticoagulants, was advocated. Although the incidence of stent thrombosis was lower, it still occurred in approximately 5% of cases and the regimen lead to the groin complications of femoral artery bleeding and pseudoaneurysm formation in up to 10%, and a prolonged hospital stay.

Richard Schatz and colleagues (1991) showed that careful attention to anticoagulation, full stent expansion and sheath removal could limit these complications to below 5% and Jean Marco noticed that stent thrombosis was less common in larger vessels (>3 mm). Subsequently in 1994, Antonio Columbo and colleagues reported that high pressure balloon dilatation (15–20 atmospheres) within the stent after placement could obviate the need for oral anticoagulant therapy (Goldberg et al, 1994). Using intravascular ultrasound (IVUS) they confirmed that high pressure dilatation ensured full stent expansion against the vessel wall and hence maintained the greatest luminal diameter.

The French Stent Registry initiated in 1992 similarly showed that with high pressure inflations, aspirin and ticlopidine alone could achieve a very low stent thrombosis rate (1%) without the need for IVUS (Morice et al, 1995). The benefits of this regimen over anticoagulant therapy were later confirmed by the prospective randomized ISAR trial in 1996 (Schomig et al, 1996).

The landmark BENESTENT (Serruys et al, 1994) and STRESS (Fischman et al, 1994) trials showed that stenting also reduced restenosis when compared to PTCA and by 1995 the era of 'stentomania' had begun. Newer low-profile, flexible stents, machine-crimped onto balloons, became available, replacing the more rigid, high-profile, hand-crimped Palmaz–Schatz device which was prone to difficulty in crossing severe lesions and complications such as stent embolization. Almost 50 different stents are now available from over 30 companies. Most are second or third generation devices with ingenious geometric designs that are evolving as stent technology advances making them easier to deliver and deploy.

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CURRENTLY AVAILABLE STENTS

A wide range of stents are now available (*Figures 1a–c*). They are more commonly balloon-expandable, e.g. Duet/Multilink® (Guidant/Advanced Systems, Santa Clara, CA) or GFX Microstent® (Applied Vascular Engineering Inc, Santa Rosa, CA), although a few are self-expanding, e.g. Wallstent® (Schneider/Boston Scientific Ltd, Maple Grove, MN) or Radius® (SCIMED/Boston Scientific Ltd, Maple Grove, MN). These latter stents are allowed to expand by retraction of a protective/constraining sheath once the stent is positioned across the lesion (*Figure 2*).

Most stents are machine-crimped on a balloon catheter — the balloon being of specific diameter (2.5–4.5 mm) and the balloon and stent of specific length (8–60 mm). The stents can often be dilated to larger than their nominal diameters by high-pressure balloon inflation after deployment. A few stents are still available as 'bare' stents which have to be finger-crimped onto the deploying balloon. The design varies from a slotted tubular mesh design, e.g. Duet/Multilink®, NIR® (SCIMED/Boston Scientific Ltd, Maple Grove, MN) or Palmaz-Schatz® (Johnson & Johnson Intervention Systems, Warren, NJ), a coil construction, e.g. Wiktor® (Medtronic Ltd, Kerkrade, Netherlands) or Gianturco-Roubin® (Cook Inc, Bloomington, IN), or a modular hoop design, e.g. AVE Microstent® (Applied Vascular Engineering Inc, Santa Rosa, CA). Some stents have been specifically designed for placement on side branches or at bifurcations, e.g. JoMed S® and JoMed B® (JoMed International AB, Helsingborg, Sweden) stents.

The radio-opacity of a stent varies according to the nature of the metal of which it is made (*Figure 3*). Stainless steel stents are difficult to visualize but those made of Tantalum are easy to see on fluoroscopy. The NIROYAL® (SCIMED/Boston Scientific Ltd, Maple Grove, MN) stent is gold-plated making it radio-opaque. The Paragon® and Radius® (Vascular Therapies, Norwalk, CT) stents are made of Nitinol. Generally, the stent is situated between two radio-opaque markers on the balloon. Some stents have small radio-opaque markers at each end of the stent itself, e.g. BeStent® (Medtronic Ltd, Minneapolis, MN).

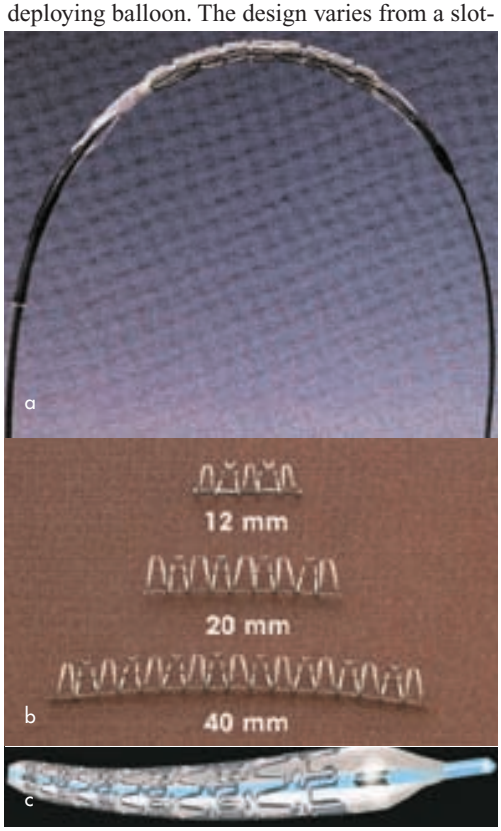

Figure 1. a. The GFX® stent (AVE-Medtronic) is a flexible stent of modular-hoop design. b. The Gianturco-Roubin® II stent (Cook) is a coil stent. Like all stents it is available in a range of sizes and lengths. c. The divYsio® stent (Biocompatibles) has a unique geometric design. Its multicellular design is clearly shown as the balloon is expanded. This particular stent is coated with phosphorylcholine.

Figure 2. The Magic Wallstent® (Schneider/Boston Scientific) is a self-expanding stainless steel mesh stent. The protecting sheath on the right has been partially withdrawn, allowing the stent to expand.

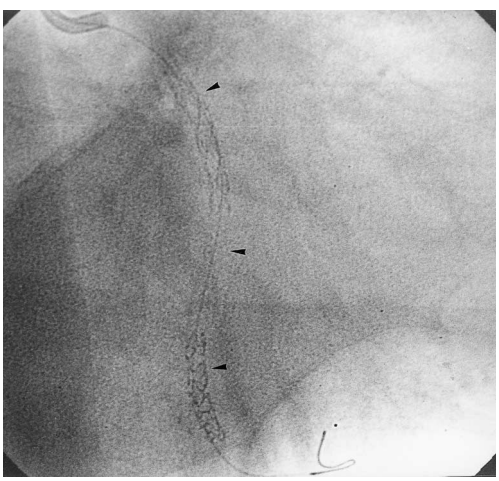

Figure 3. Fluoroscopy shows the different radio-opacity of three stents placed sequentially within the left circumflex coronary artery (arrows). From top to bottom these are a 3.5 mm 30 mm long Microstent II® (AVE-Medtronic) stent, a 3.0 mm 25 mm long Multilink® (Guidant) stent and a 3.0 mm 16 mm long Wiktor i® (Medtronic-AVE) stent.

The different geometric designs and metal: artery ratio give the various stents differing flexibility, trackability, radial strength and wall support. Biliary stents can be used for large vessels and vein grafts.

Stents can be coated with heparin, e.g. Palmaz-Schatz® or Wiktor Hepamed®, with silicon carbide, e.g. Tenax® (Biotronic, Berlin, Germany), or with phosphorylcholine, e.g. divYsio® (Biocompatibles, Farnham, UK), in an attempt to limit platelet adhesion and eliminate subacute thrombosis. Polytetrafluoroethylene (PTFE)-covered stents are also available, e.g. JoMed Stent Graft®, which may be useful for sealing coronary artery perforations and coronary artery aneurysms after intervention and for lesions in saphenous vein grafts. The detailed characteristics of stents that are currently or recently available have been well described (Serruys and Kutryk, 1998; Kutryk and Serruys, 1998). Stents are expensive, costing between £350 and £900 each.

CURRENT INDICATIONS

Coronary artery stent implantation is indicated:

1. For an unsatisfactory result after PTCA because of:
   a. Coronary artery dissection/occlusion
   b. Lesion recoil
2. Electively
   a. In high-risk lesion subsets, e.g. complex, bulky, ulcerated, eccentric lesions, lesions on bends which are at higher risk for dissection and acute closure and in acute myocardial infarction (so-called primary stenting)
   b. In saphenous vein grafts to reduce restenosis
   c. To reduce restenosis in de novo lesions, restenosis lesions, chronic total occlusions, ostial lesions.

Generally, coronary arteries <2.5 mm in diameter should not be stented and although there may soon be available stents of 2.0 mm diameter for small calibre (2.0–2.5mm) vessels (BiodivYsio SVPC stent, Biocompatibles Ltd, Farnham, UK), the restenosis rates in such small vessels may be a problem. Lesions that are heavily calcified or that cannot be adequately dilated should not be stented and extremely tortuous vessels, very distal lesions and vessels heavily laden with thrombus should be avoided.

PROCEDURE

As with any PTCA, the patient should be receiving aspirin 150 mg daily before the procedure. For emergency PTCA/stenting, a 600 mg loading dose of aspirin is usually given immediately. Heparin 10 000U intravenously is given just before PTCA and may be continued for 12–24 hours afterwards if clinically indicated.

Usually, after crossing the lesion with an angioplasty guidewire the stenosis is predilated with a balloon catheter before stenting. This should make it easier for the balloon-mounted stent to cross the lesion more easily without damaging or displacing the stent. Moreover for hard, calcific or balloon-resistant lesions 'attempted predilatation' allows the operator to use other technology, e.g. Rotablator® (Boston Scientific Ltd, Maple Grove, MN), before stent implantation and avoids the potentially disastrous 'partially-deployed stent' scenario.

Studies are currently underway to assess how frequently and how safely 'primary stenting' (stenting without predilatation) can be performed in practice now that low-profile devices are available.

The stent is usually deployed at 10–12 atmospheres. The balloon catheter is then withdrawn and the stent is post-dilated with a slightly shorter balloon (within the stent) up to 16–18 atmospheres. IVUS may assist in ensuring optimal stent deployment (Columbo, 1997).

In the catheter laboratory, once the decision is made to deploy a coronary stent the patient is given clopidogrel 150 mg orally and 75 mg daily thereafter for 1 month in addition to aspirin 150 mg daily.

Figures 4a and *b* shows a diagrammatic representation of a stent crimped onto a balloon being placed within a coronary artery and then deployed. *Figure 5* shows a complex, bulky right coronary artery lesion before, during and

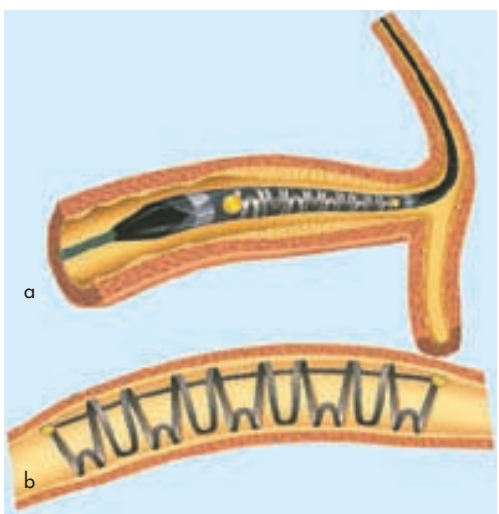

Figure 4. a. Diagrammatic view of a stent crimped onto a balloon catheter being delivered into the coronary artery. b. Stent deployed against wall of artery and balloon catheter withdrawn.

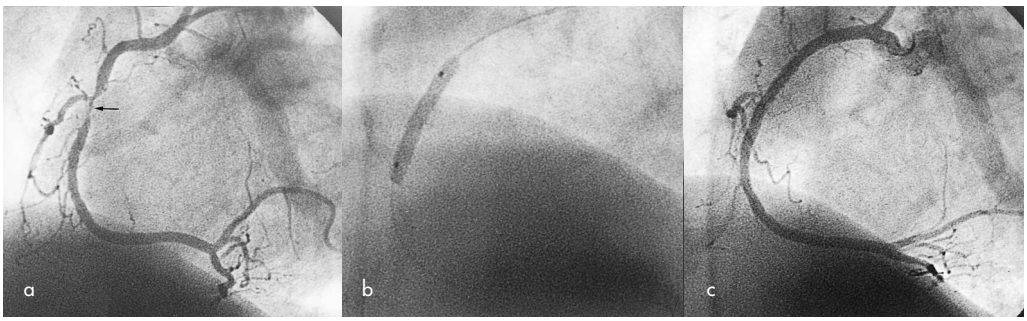

Figure 5. Severe complex, bulky stenosis (arrow) in the proximal right coronary artery. a. Before stent deployment. b. During stent deployment. c. After stent deployment.

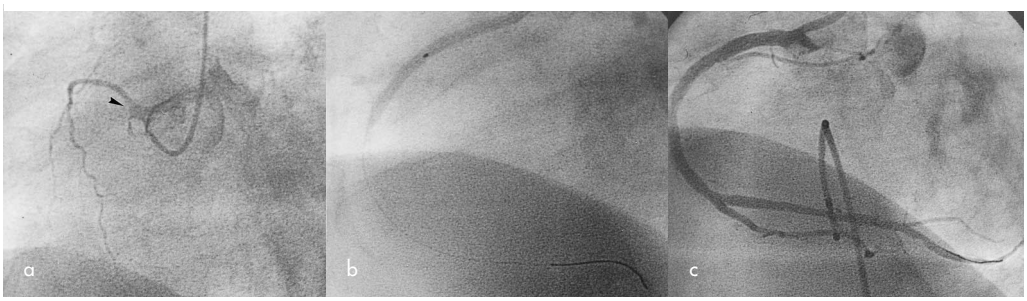

Figure 6. Totally occluded right coronary artery (arrow). a. Before. b. During. c. After stent deployment.

after stent implantation. *Figures 6a–c* shows the result of PTCA and coronary stent implantation to a totally occluded right coronary artery. *Figures 7a* and *b* shows the dramatic improvement in a stenosis in a saphenous vein graft to a left anterior descending coronary artery after stent implantation.

Stenting can be used as an adjunct to directional or rotational atherectomy for specific lesion subsets as shown in *Figures 8a–c* and *9a–c*.

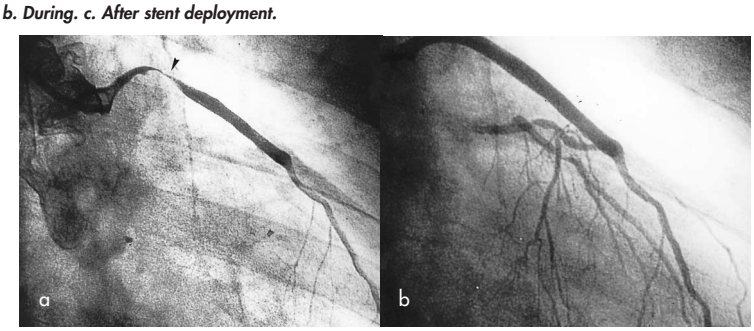

Figure 7. a. Severe stenosis (arrow) in proximal portion of saphenous vein graft to left anterior descending coronary artery. b. Appearance after percutaneous transluminal coronary angioplassty and stent deployment.

RESULTS

Successful deployment occurs in 95–100% of cases and depends on the experience of the interventionist, the coronary anatomy and the lesion morphology being addressed. Acute thrombosis occurs in <1% of cases.

In 1994, the large prospective randomized trials BENESTENT and STRESS showed conclusively the superiority of elective stenting over PTCA in clinical and angiographic outcomes. The lumen diameter after stenting was greater and the restenosis rates at 6-month follow-up were lower. BENESTENT II using a heparin-coated stent showed a subacute thrombosis rate

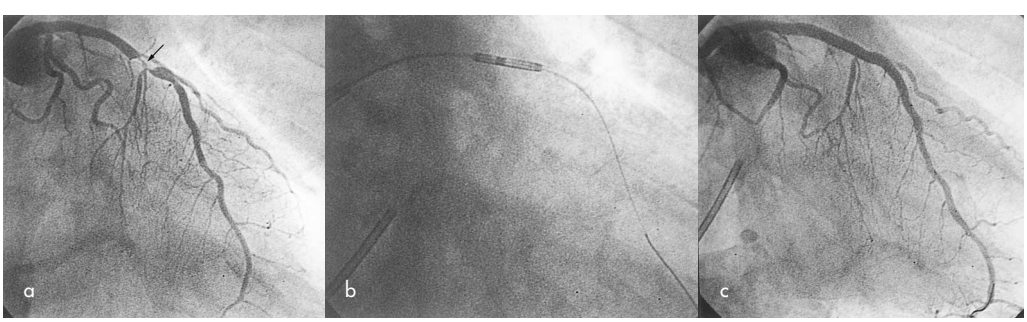

Figure 8. a. Severe stenosis (arrow) in proximal left anterior descending coronary artery. b. During directional coronary atherectomy (DCA). c. After DCA and stent implantation.

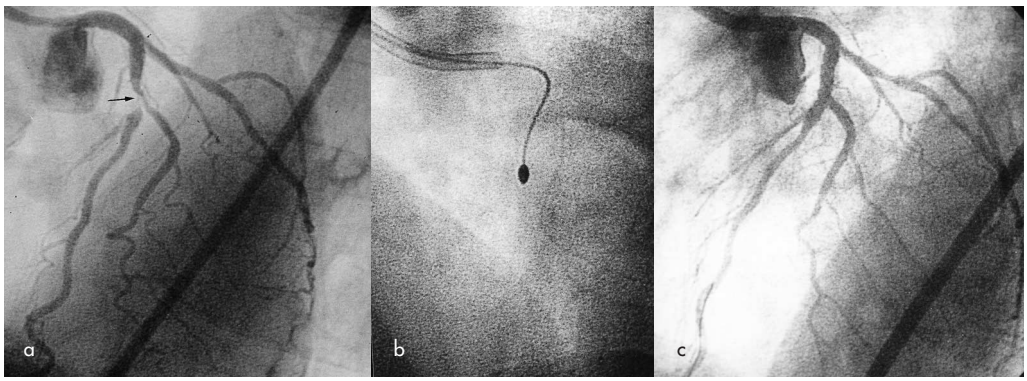

Figure 9. a. Severe bifurcation stenosis (arrow) at junction of left anterior descending and diagonal coronary arteries. b. During rotational atherectomy with the Rotablator® device. c. After stent implantation to both vessels at bifurcation point.

of 0.2% and a restenosis rate of 17% compared to 31% for PTCA.

Numerous trials looking at the many aspects of stenting in clinical practice have been concluded and many are still ongoing (Kutryk and Serruys, 1998). For example, the SAVED trial showed the benefits over PTCA in saphenous vein grafts and the REST trial showed benefits over PTCA for treating restenosis lesions. The SICCO trial showed that stenting for chronic total occlusions provided better long-term outcome than PTCA alone and the TASC II trial showed a higher clinical and angiographic success rate for patients with failed PTCA treated by stenting compared to those treated by prolonged inflations with the autoperfusion balloon. In acute myocardial infarction, the GRAMI, PASTA, ESCOBAR, FRESCO and PAMI-STENT trials have shown extremely high primary success rates after stenting as well as lower rates of target vessel revascularization and higher cardiac event-free survival rates at 6 months than after PTCA alone.

Other trials have evaluated the benefits of combining certain drugs with stenting in differing clinical situations, e.g. EPISTENT, ERASER and CADILLAC (abciximab), ISAR and STARS (anticoagulants) and CLASSICS (clopidogrel, ticlopidine and aspirin). Others are evaluating the comparative benefits of stenting *vs* coronary artery bypass surgery for patients with multivessel disease (ARTS and SOS) and others the value of intracoronary irradiation after stent implantation for reducing in-stent restenosis (SCRIPPS I and II, IRIS and WRIST). The AMIGO trial is studying the benefits of combining directional coronary atherectomy with stenting and the ROSTER and ARTIST trials are examining the effectiveness of rotational atherectomy for the treatment of in-stent restenosis. The SPORT trial is assessing the value of rotastenting for the treatment of coronary disease.

COMPLICATIONS

It may be impossible to reach the lesion because of tortuosity in the vessel or because of disease or calcification in the artery proximal to the lesion. Low-profile, flexible coil stents may track around bends more easily. It may be necessary to predilate proximal disease or even use rotational atherectomy in order to allow stent passage to the lesion site. Difficulty crossing the lesion should be helped by predilatation but sometimes atherectomy may be required.

Stents can be displaced from their deployment balloon and can be lost in the coronary artery or elsewhere in the circulation. It is only possible to attempt retrieval if the stent can be seen on fluoroscopy.

Balloon rupture can sometimes be problematic and edge tears or dissections usually require further stent deployment proximally or distally as necessary.

Inadequate stent expansion as a result of lesion resistance is a serious problem. It can sometimes only be confirmed by IVUS. High pressure balloon dilatation is necessary but inadequate expansion is a predisposing factor for stent thrombosis.

Subacute/acute stent thrombosis probably occurs in <1% of cases now that aspirin and clopidogrel are used and stents are properly deployed at high pressure. Small calibre vessels (<3.0 mm), multiple stents in sequence, bail-out stents, inflow or outflow obstruction, inadequate stent expansion, thrombus-associated lesions and the use of warfarin anticoagulation may predispose to stent thrombosis. It carries a significant risk of myocardial infarction and a mortality rate of 3–5%. Although it can occur in the catheter lab, it is then unusual in the next 24 hours. It may occur on the second day, but the peak incidence is on day 4–6. It can occur up to 4 weeks following stent

insertion but is then most unlikely. Bleeding complications on the antiplatelet regimen are unusual (1–2%).

When a stent placed in a main vessel is positioned across a side branch and the side branch cannot be accessed because of obstructing stent struts, the side branch is said to be in 'stent-jail'. It is less of a problem with coil stents.

In-stent restenosis, although uncommon, is a major problem when it happens. It occurs most commonly 3–6 months after implantation. The intimal hyperplasia response induced by a stent is greater than that after PTCA and so it is imperative to obtain the largest luminal diameter possible after stent deployment in order to minimize the effect of 'late loss' resulting from intimal hyperplasia.

Risk factors for in-stent restenosis include diabetes mellitus, multiple stents for long diffuse disease or treatment of dissection, long stents, final lumen diameter <3.0 mm, small arteries and stenting in occluded vessels. Treatment is difficult because of a high incidence of recurrent restenosis but includes PTCA, rotational, excimer laser or directional atherectomy and deployment of a second stent within the first stent. Covered stents might have a role to play here too. Intrastent irradiation after stent deployment might prevent this complication and might also be useful treatment for the complication itself.

Stent infection is rare but potentially lethal.

COST CONSIDERATIONS

Although the initial cost of a stent procedure is higher than that of PTCA alone, the cost is offset by a shorter hospital stay and a lower requirement for reintervention in the first year of follow-up.

FUTURE DEVELOPMENTS

The use of coronary stents will continue to increase in the near future as the indications expand and the results of randomized trials become available. The ability to coat stents with new biocompatible polymers and drug-eluting polymers is being intensely investigated. Biodegradable polymers which can be loaded with antithrombotic or antiproliferative agents could be usefully applied to stents to prevent thrombosis and restenosis.

A promising advance has been the development of stents which provide locally active ionizing radiation which have the potential to inhibit the restenosis process completely. Stents are being designed specifically for small vessels, bifurcation lesions and ostial lesions and the first generation of covered stents have already appeared. With continued research and development and refinements, stenting will continue to be an important part of the interventionist's armamentarium for the management of coronary artery disease. **HM**

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KEY POINTS

- Coronary artery stenting is indicated for an unsatisfactory result after percutaneous transluminal coronary angioplasty as a result of dissection or recoil, lesions at higher risk of dissection and acute closure, acute myocardial infarction and reducing restenosis, e.g. saphenous vein graft lesions.
- A wide variety of stents are now available of various geometric designs, lengths, diameters, radiopacity, flexibility and radial strength.
- Stents should be fully deployed by high balloon inflation pressure, with intravenous ultrasound guidance if necessary.
- Subacute thrombosis is now rare with correct deployment techniques and antiplatelet therapy.
- Numerous clinical trials have been performed and are currently ongoing to assess the value of stents in a variety of clinical situations and in synergy with other devices.